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ABSTRACT

Techniques for detecting synergistic effects in analysis of variance designs are presented and discussed. These techniques make it possible to apply some kinds of theoretical insights to the data analysis phase of a study: either by seeking synergistic effects implied or predicted by theory, or by seeking evidence of synergies as alternative explanations for results which would otherwise imply the existence of interactions where theory would deny such interactions. In complex factorial designs particularly, where high-order interactions are often called "uninterpretable," these techniques may often permit more appealing explanations and interpretations of the experimental results. (Author)

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SYNERGISTIC EFFECTS IN THE ANALYSIS OF VARIANCE

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Introduction

One occasionally comes across papers suggesting various kinds of nonlinear transformations of observed data in an experiment, as a means of reducing or eliminating effects attributable to interaction among the factors of the experimental design; such procedures seem especially to be advocated where the interactions found in the original data are difficult to interpret. While there may sometimes be good reasons for examining transformations of the data (reasons related, e.g., to deep questions about the nature and meaning of the measured variable), it is probably unwise to attempt to eliminate interactions solely because of interpretative difficulty: the data, after all, may be trying to tell the investigator something! An alternative approach is presented here: Because the compactness and efficiency of complete balanced designs arise from the use of every available cell mean in the estimation of every effect implied by the formal design, one cell which is systematically atypical (or "strange") with respect to the other cells can contaminate all reported sources of variation in the usual analysis of variance (ANOVA) summary table. It follows that if that cell can be identified, and its mean "adjusted" for the suspected "strangeness," the summary table can be similarly adjusted and the resultant pattern of significant effects compared with the originally obtained pattern. If the new results are more consistent with theoretical arguments, and if the strangeness implied in the "adjusted" cell also makes some theoretic sense, then an hypothesis asserting the existence of "strangeness," or of a synergistic effect, in that cell is tenable.

(Since in general that particular hypothesis will be only one among many alternative hypotheses, some of which may be equally attractive, the proper outcome in most cases will be a new experiment designed specially to distinguish among these competitors. Only rarely will an unequivocal explanation be clearly implies by the data; and, usually, such explanations will be evident without a statistical analysis.)

S y n e r g i s t i c e f f e c t s

For the purposes of this discussion, a synergy, or synergistic interaction, is taken to mean a unique effect in a single cell of an ANOVA design, which acts to change the value of the population mean in that cell (but not in others), and does not affect the within-cell variation about the cell mean. In effect, postulating a synergy in a design amounts to adding another term to the ANOVA model while deleting one of the usual terms of the model (in a 2^k design) or removing one degree of freedom from one of the usual terms (when there are factors with more than two levels).

By way of illustration, consider an electrical circuit containing a battery, a light bulb, and three switches, all connected in series. Each switch has two positions (labelled, perhaps, "high" and "low") and corresponds to a two-level design factor. Only when all three switches are in their respective "on" positions (which may or may not correspond to the label "high") does electric current flow through the circuit and cause the bulb to glow. (The dependent variable corresponds either to the illumination provided by the bulb, or to the amount of current flowing in the circuit). For any other settings of the switches -- i.e., if any one or more of them are "off" -- no current will flow and the bulb will remain unlit. Again, in a circuit containing a battery and a bulb in series with a set of three switches, but where the switches are

connected in parallel, current will flow and the bulb will light up unless all three switches are "off."

On catalysis

Neale and Liebert (1973, page 63), in what appears to be an egregious misunderstanding of the nature of catalysis in chemistry, use the term "catalytic interaction" to describe the situation wherein "two or more treatments are effective only when they occur together." The paradigm is an experimental outcome in which the value of the dependent variable is constant over all cells of a design, with one exception; in the exceptional cell the dependent variable takes on a substantially different value.[1] Since in such a paradigm there is no obvious rôle for a "catalyst," in the sense of a substance (or an analogue of a substance) whose presence is necessary for the reaction (interaction) to occur but which is itself unchanged by the reaction, the term *synergistic interaction* (or, more simply, *synergy*) is preferred herein to describe the case of a dependent variable whose value changes sharply as an apparent result of the coincidental occurrence of particular values of each independent variable. While the notion is clearly extensible to synergies in a number of cells in a design, this paper is addressed only to detecting and interpreting a synergy in one cell; the simultaneous existence of real main effects and of some non-synergistic interactions is permitted, however.

An arbitrary (hypothetical) example

Imagine a 2^3 ANOVA design in which there are no differences in cell means for seven of the eight cells, but the eighth cell is remarkably (in the sense of Saunders (1970)) different from the others. Because all the sources of variation reported in the ANOVA are equivalent to single contrasts comparing

four of the cells to the other four cells, the exceptional cell (and it alone) will contribute to all seven sources of variation reported in the standard ANOVA: A, B, C, AB, AC, BC, and ABC. If any effect is significant, all are significant. Such a situation is depicted in Figure 1(a), with artificial "data" reported in Table 1(a). In this case, it is clearly more parsimonious, and probably more informative for the development of theory, to describe the observed pattern of results as due to a single synergy among the three design variables, rather than as reflecting seven independent sources of variation. (Of course, it is impossible purely on the basis of the data to distinguish between the two explanations; both "explain" the results equally quantitatively. One may prefer one explanation or another on the basis of parsimony, theory, or sheer intuition, but a specially designed experiment would be required to make an empirical (or statistical) distinction.)

Now suppose the situation is the same as just described, but there is also a 'true' main effect due to factor B, in the opposite direction to the 'spurious' effect caused by the synergy in cell (122). Then the variation attributed to B in the ANOVA is reduced (in the present case, eliminated altogether because of using a 'true' effect equal in size to the 'spurious' effect), but the other six sources remain 'significant' in the ANOVA. This case is shown in Table 1(b) and Figure 1(b). The addition of other 'true' effects to the design will either increase or diminish the reported strength of the effects, depending on whether the 'true' effects are in the same direction as the 'spurious' effect generated by the synergy, or in the opposite direction. As more 'true' effects are added, the 'spurious' effect of the synergy is more and more concealed by the real effects; eventually it becomes more parsimonious (but not necessarily truer) to interpret the data in terms of the ordinary ANOVA results than in terms of a synergy plus some 'real' effects. See Table 1, (c)

to (h), and Figure 1 (c) to (h). [The dashed lines in Figure 1 represent the patterns that would have been observed had no synergy been present.]

By the time we get to cases (d) and (e) in Table 1, it is difficult to discern a clear synergy in the tables, although the effect is somewhat more apparent in Figure 1. Among the strategies that might be used to make the strangeness of cell (122) more visible are (i) representing the values in each cell as deviations from the smallest cell mean and (ii) representing them as deviations from the grand mean of the observed values. Strategy (i) is shown in Table 1, (a') to (h'); strategy (ii) by Table 1, (a") to (h"). Up to about cases (d) and (e) the deviations suggest a 'strangeness' about cell (122), but the suggestiveness decreases as more 'real' effects are added.

Detection of synergies

From the definition given above (see page 2), the detection of a synergy is equivalent to the estimation of the change in the value of a cell mean as a result of the proposed synergy. The estimation requires one degree of freedom, which must be found among the degrees of freedom associated with treatments. In 2^k designs, detection of a synergy therefore requires assuming that one of the usual sources of variation does not exist. Since an assumption of this kind is often implied by underlying theoretical arguments (or made tacitly by the investigator) with respect to higher-order interactions, the requirement is unlikely to be prohibitive, especially for $k > 3$. Where design variables have more than two levels, the required degree of freedom may be obtained by imposing some constraint(s) on one or more sources of variation, rather than requiring one source to disappear altogether.

For 2^k designs the following procedure is simple and straightforward: first, select a source of variation which "ought" not to exist (the selection

may be based on various criteria: a theory that implies absence of a particular interaction (or main effect, for that matter), or starting with the smalles reported mean square, for example). In a 2^k design, this source will have one degree of freedom. Write the formal contrast representing this source, set it to zero, and solve for the mean of a selected cell in terms of the other cell means. (As before, selection of the cell may be based on various criteria.) The effect of this procedure is to attribute all variation apparently due to a particular source -- a line in the usual ANOVA table -- to a synergy, and to use the degree of freedom usually associated with that source to estimate the size of the synergy. Finally, recalculate the ANOVA, using the newly calculated cell mean instead of the original value in the cell selected for adjustment, and compare the pattern of results with that obtained from the raw data. If the new results are more satisfying in terms of theoretical considerations, and a synergy in the particular cell selected makes some kind of sense, and if the new results are more parsimonious than the original (in the sense either of requiring fewer sources to explain the variation observed, or of producing a smaller value for the total treatment sum of squares (SS_{Tr}), then a synergy in the selected cell is a tenable hypothesis.

There may, however, be other tenable hypotheses meeting these criteria; it is therefore to be recommended that the procedure just described with respect to one selected cell in the design be repeated with each of the other cells in turn. If more than one tenable hypothesis results (which will nearly always be the case, since the usual ANOVA sources of variation presumably represent an *a priori* set of tenable hypotheses), the task is then to design one or more experiments which will be capable of distinguishing among the several hypotheses.

The procedures just described may most easily be understood by considering their application to some real data.

An empirical example

In an experiment investigating the degree to which individuals display understanding of logical principles and their application to a certain kind of inferential problem, Bracewell and Hidi (1973) observed that in one of their eight ($= 2^3$) conditions nearly perfect performance routinely occurred, while the other seven conditions displayed substantially poorer performance (with systematic differences among them). The ANOVA summary indicated significant main effects due to factors A and C of the three-way design, and no effect due to B, all more or less as expected; but in addition a significant BC interaction was reported which was unexpected and difficult to interpret. There was, however, a reasonable basis for interpreting the superior performance in the one cell mentioned above; under the suspicion that performance in this cell might be sufficiently unlike that in the other cells to generate a spurious interaction, an "adjusted" mean for that cell was calculated, on the basis of denying the presence of a three-way interaction.[2] The original data are reported in the second line of Table 2, labelled "Raw Mean," and are displayed graphically in Figure 2. The original sum of squares (SS) for each source of variation appears in the rightmost column of Table 2, in lines 1-7; their sum appears in line 8 as SS_{Tr}.

Using the "adjusted" value for cell (111), the ANOVA was repeated. The adjusted mean is indicated in the lower part of Table 2, and the contrast values representing each source of variation appear in the column beneath the adjusted mean. Again the main effects A and C were significant (both less strongly than before), but there were no other significan effects. All mean squares were smaller than they were originally; those for effects B, AB, AC, and BC ranged from 0 to 31% of their original values; expressed in terms of the error mean square (MS_E) the absolute decrements in mean squares for these

four effects ranged from 1.36 MS_E to 4.78 MS_E. Also, SS_{Tr} was considerably reduced, from 275.5 to 111.5, about 40% of its original value. The postulated synergy, therefore, could be said to account for 60% of the total SS_{Tr}, with a SS of 164.0, considerably larger than any other effect; even though the actual difference in the cell mean was only 8, the value of the original ABC contrast.

At first glance, these results seemed impressive evidence for the existence of a unique effect in cell (111), which might be explained in terms of a synergy representing the action of the three factors in the design. To see whether such a synergy operating in some other cell of the design might be an equally attractive explanation of the behaviour of the data, the same procedure was applied to every other cell. The adjusted means and adjusted contrast values (in lieu of the several SS's) appear in the lower part of Table 2, together with the value of SS_{Tr} on line 8. Each set of means, with one cell mean adjusted, is displayed in Figure 2. Besides allowing comparisons among all possible unique effects as possible explanatory devices, the procedure also permits examining the pattern of siginificant effects, to see (e.g.) whether the main effects A and C always turned up, or whether one or the other of them also disappeared under some hypothesized synergies. As Table 2 shows, these two main effects always showed up, with A usually stronger than C; and in all cases except adjusting cell (111), at least one other effect appeared (and usually at least one of these additional effects were significant at the .01 level). On the basis of parsimony, then, one would prefer the original hypothesis that a unique effect or synergy was operating in cell (111), together with two easily interpretable main effects, and no interactions other than the synergy; since any other synergy requires one or more interactions to exist.

Another possible criterion is the total SS_{Tr} resulting from adjustment of a cell mean. While it is possible to imagine a unique effect operating in such a way as to mask or suppress real general effects (main or interactions) due to the design factors, and therefore to reduce the total SS_{Tr} reported in the original ANOVA table from what that total "ought" to be, one would need compelling substantive or logical reasons to accept the existence of such a "suppressor." Ordinarily, one would expect a parsimonious explanation to reduce the adjusted SS_{Tr} to a lower value than the original value. On examining Table 2, we see that in all cases except cells (111) and (222) the SS_{Tr} after adjustment is larger than before -- by amounts ranging from 6.14 MS_g to 26.60 MS_g. Since in this case the compelling reasons supported cell (111) rather than any others, and since adjusting cell (111) both reduces SS_{Tr} the most and results in the smallest number of significant effects, the most satisfying explanation of the original data adduces a synergy or unique effect in cell (111) plus main effects due to factors A and C.

Extension to several contrasts

In the case of designs involving factors with more than two levels, the usual ANOVA sources of variation will have more than one degree of freedom. For such cases the same kind of procedure and reasoning apply as for 2^k designs; but having selected a source of variation which "ought" not to exist (or which the investigator wants to minimize) and which has f degrees of freedom, one may either write the total SS for that source as an explicit function of the cell means, and then minimize the SS with respect to each cell mean in turn; or one may write the SS as a sum of D_i^2, $i = 1, \cdots, f$ (see, e.g., Guenther, 1964, §2-12) corresponding to f orthogonal contrasts, set one of those contrasts to zero, and solve for the cell mean(s) to be adjusted. In either case there remain $f-1$ degrees of freedom for variation due to that source

above and beyond the effects of the hypothesized synergy. As for the 2^k designs, results of adjusting for hypothetical synergies would be evaluated in terms of parsimony of significant effects, parsimony of total SS_{Tr}, implications for theory of synergies in particular cells, and general interpretability; and since this is a variety of *post hoc* analysis, such evaluations ought in general to lead to refined experimental designs and additional hypotheses to be tested rather than to firm conclusions.

The principle of minimizing a SS having f degrees of freedom with respect to a cell mean logically implies the possibility of minimizing a SS composed of several sources of variation with respect to a cell mean. While no obvious examples spring immediately to mind where a procedure of this kind would be appropriate, such examples may exist.

Rules of thumb

The procedures described in this paper for detecting synergistic effects in analysis of variance designs are summarized in the rules of thumb displayed in Table 3.

Implications

Ordinarily, the impact of substantive theory on an experimental study is largely limited to the design of the experiment: the number and selection of the design variables, the number and selection of discrete levels (values) of each variable, and perhaps specification of the effect size (see Cohen, 1973) against which reasonable power is desired. After the experiment has been carried out and the data have been analyzed, the investigator typically attempts to explain the results of the ANOVA in the light of theory, or (s)he may attempt to illuminate (or modify) theory on the basis of the experimental results. The analysis of data, however, is typically carried out in a purely formal (not to

say mechanical) way, without reference to the substantive area of the investigation nor, often, to theory which may imply certain expectations about the results.

The techniques discussed in this paper make it possible to apply some kinds of theoretical insights to the data-analysis phase of a study: either by seeking synergistic effects implied or predicted by theory, or by seeking evidence of synergies as alternative explanations for results which would otherwise imply the existence of interactions where theory would deny such interactions. In complex factorial designs particularly, where high-order interactions are often called "uninterpretable," these techniques may often permit more appealing explanations and interpretations of the experimental results.

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N O T E S

[1] Neale and Liebert (1973) also define "terminative interactions," wherein "two or more variables are clearly effective in modifying behavior, but, when combined, their effect is not increased over what either alone could do." Analytically, this is not different from a "catalytic interaction": the apparent difference seems to depend wholly on whether one starts by considering pairwise cell contrasts which are substantially (or "clearly"?) different from zero, or by considering contrasts which are not different from zero; and possibly on whether the non-zero contrasts are "positive" or "negative." Such distinctions appear unreasonably arbitrary.

[2] Notice that the original, or "raw," three-way interaction was one of the two smallest effects in the analysis (the other being the AB interaction). Observing that the original ABC contrast had the value 8, we see that the "adjustment" consists in subtracting 8 from cell (111), since the contrast coefficient for that cell in the ABC contrast was +1. Similarly, the adjusted mean for each other cell is either 8 less or 8 more than its "raw" value, depending on whether its coefficient in the ABC contrast was +1 or -1. Incidentally, another check on the reasonableness of an hypothesis of synergy is the adusted mean in a given cell; if it is "adjusted" out of the possible range of observable values, the hypothesis is a little hard to take! Since in the present example the minimum possible cell mean was 12, three of the "synergies" examined are in this sense nonsensical.

TABLE 1. An Arbitrary (Hypothetical) Example.

	A_1		A_2							
	B_1	B_2	B_1	B_2						
(a)					(a')				(a")	
C_1	10	10	10	10		0	0	0	0	$-2\frac{1}{2}$ $-2\frac{1}{2}$ $-2\frac{1}{2}$ $-2\frac{1}{2}$
C_2	10	30	10	10		0	20	0	0	$-2\frac{1}{2}$ $+17\frac{1}{2}$ $-2\frac{1}{2}$ $-2\frac{1}{2}$
(b)	15	10	15	10	(b')	5	0	5	0	(b") 0 -5 0 -5
	15	30	15	10		5	20	5	0	0 $+15$ 0 -5
(c)	20	15	20	15	(c')	10	5	10	5	(c") $+2\frac{1}{2}$ $-2\frac{1}{2}$ $+2\frac{1}{2}$ $-2\frac{1}{2}$
	15	30	15	10		5	20	5	10	$-2\frac{1}{2}$ $+12\frac{1}{2}$ $-2\frac{1}{2}$ $-7\frac{1}{2}$
(d)	25	20	20	15	(d')	15	10	10	5	(d") $+5$ 0 0 -5
	20	35	15	10		10	25	5	0	0 $+15$ -5 -10
(e)	20	15	25	10	(e')	5	0	10	5	(e") 0 -5 $+5$ 0
	15	30	20	15		0	15	5	0	-5 10 0 -5
(f)	25	15	25	25	(f')	10	0	10	10	(f") $+2\frac{1}{2}$ $-7\frac{1}{2}$ $+2\frac{1}{2}$ $+2\frac{1}{2}$
	20	30	20	20		5	15	5	5	$-2\frac{1}{2}$ $+7\frac{1}{2}$ $-2\frac{1}{2}$ $-2\frac{1}{2}$
(g)	30	20	25	25	(g')	10	0	5	5	(g") $+5$ -5 0 0
	20	30	25	25		0	10	5	5	-5 $+5$ 0 0
(h)	30	25	25	30	(h')	5	0	0	5	(h") $+2\frac{1}{2}$ $-2\frac{1}{2}$ $-2\frac{1}{2}$ $+2\frac{1}{2}$
	25	30	30	25		0	5	5	0	$-2\frac{1}{2}$ $+2\frac{1}{2}$ $+2\frac{1}{2}$ $-2\frac{1}{2}$

No 'true' effects, but one synergy in cell (122).
ANOVA: All seven sources significant.

Add a 'true' B effect, opposite in sign to the synergy.
ANOVA: as in (a), but no B effect.

Add a 'true' C effect, opposite.
ANOVA: A, AB, AC, BC, ABC are significant.

Add a 'true' A effect, same direction.
ANOVA: as in (c), with a stronger A effect.

Add a 'true' A effect to (c), opposite.
ANOVA: no main effects, but all interactions significant.

Add a 'true' AB effect, opposite.
ANOVA: BC, AC, ABC significant.

Add a 'true' AC effect, opposite.
ANOVA: BC, ABC significant.

Add a 'true' BC effect, opposite.
ANOVA: Only ABC significant.

TABLE 2. An Empirical Example (Bracewell & Hidi, 1973)

	Cell:	111	112	121	122	211	212	221	222	Contrast Value, $\hat{\psi}_j$	$n\,SS_j$, $\hat{\psi}_j^2/8$
	Raw Mean:	32	17	21	19	17	12	14	14		
j	Source of Variation	Contrast Coefficients									
0	Grand Mean (C.T.)	1	1	1	1	1	1	1	1	146	2664.5
1	A	1	1	1	1	-1	-1	-1	-1	32	128.0**
2	B	1	1	-1	-1	1	1	-1	-1	10	12.5
3	C	1	-1	1	-1	1	-1	1	-1	22	60.5**
4	AB	1	1	-1	-1	-1	-1	1	1	8	8.0
5	AC	1	-1	1	-1	-1	1	-1	1	12	18.0
6	BC	1	-1	-1	1	1	-1	-1	1	18	40.5*
7	ABC	1	-1	-1	1	-1	1	1	-1	8	8.0
8	Treatments										275.5

	Adjusted Mean:	24	25	29	11	25	4	6	22
j	Source of Variation	Adjusted Contrast Value, $\hat{\psi}_j$							
0	Grand Mean (C.T.)	138	154	154	138	154	138	138	154
1	A	24**	40**	40**	24**	24**	40**	40**	24**
2	B	2	18*	2	18*	18*	2	18*	2
3	C	14*	14*	30**	30**	30**	30**	14*	14*
4	AB	0	16*	0	16*	0	16*	0	16*
5	AC	4	4	20**	20**	4	4	20**	20**
6	BC	10	10	10	10	26**	26**	26**	26**
7	ABC	0	0	0	0	0	0	0	0
8	$SS_{Treatments}$	111.5	311.5	375.5	319.5	311.5	431.5	399.5	263.5

* $F_{1,88} > 3.96$, $p < .05$; $|\hat{\psi}| > 13.63$.

** $F_{1,88} > 6.94$, $p < .01$; $|\hat{\psi}| > 18.04$.

$n\,MS_E = 5.864$.

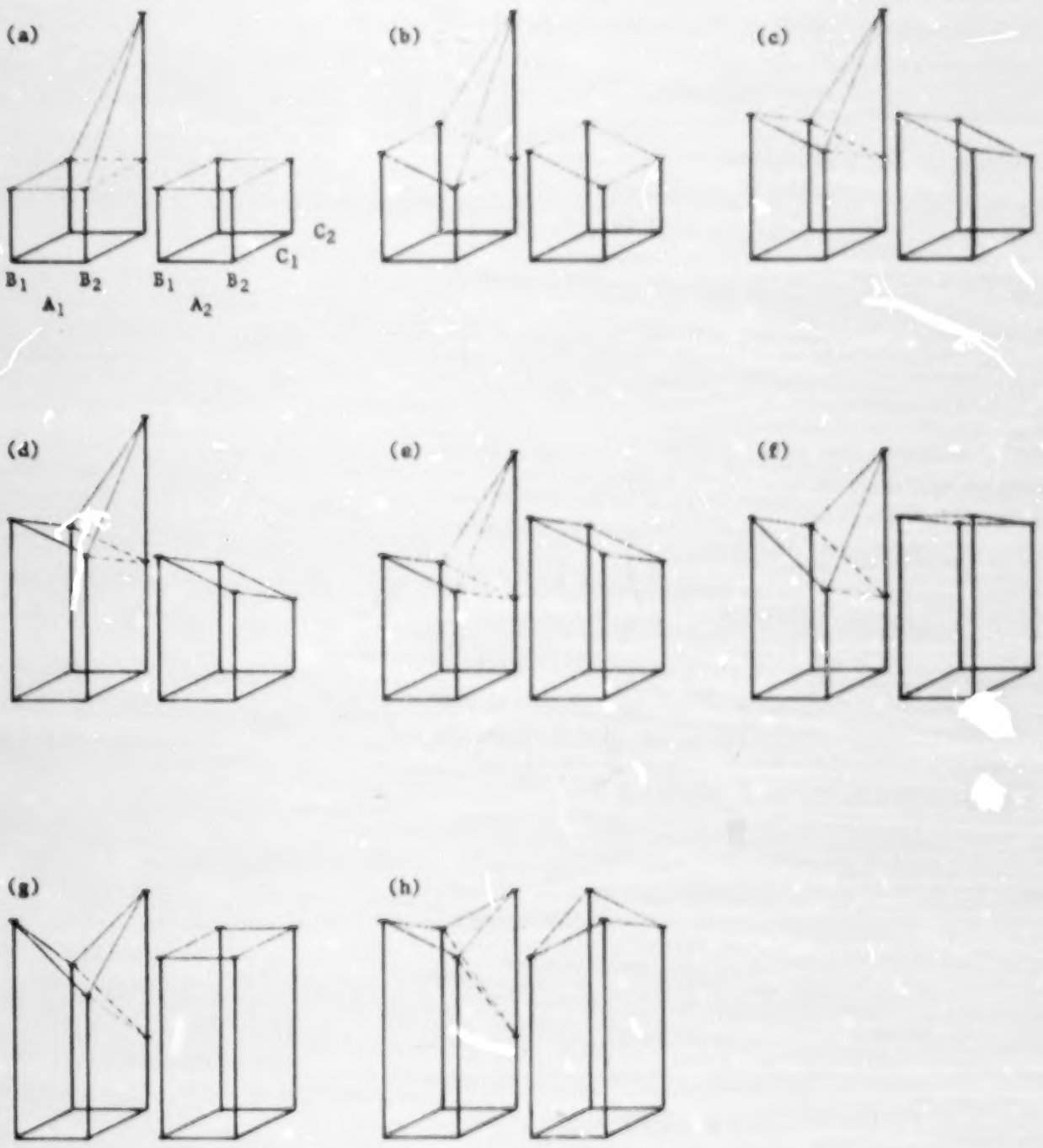

FIGURE 1. An Arbitrary Example. Data from Table 1.

[Dotted lines indicate relationships that would occur in the absence of the synergy in cell (122).]

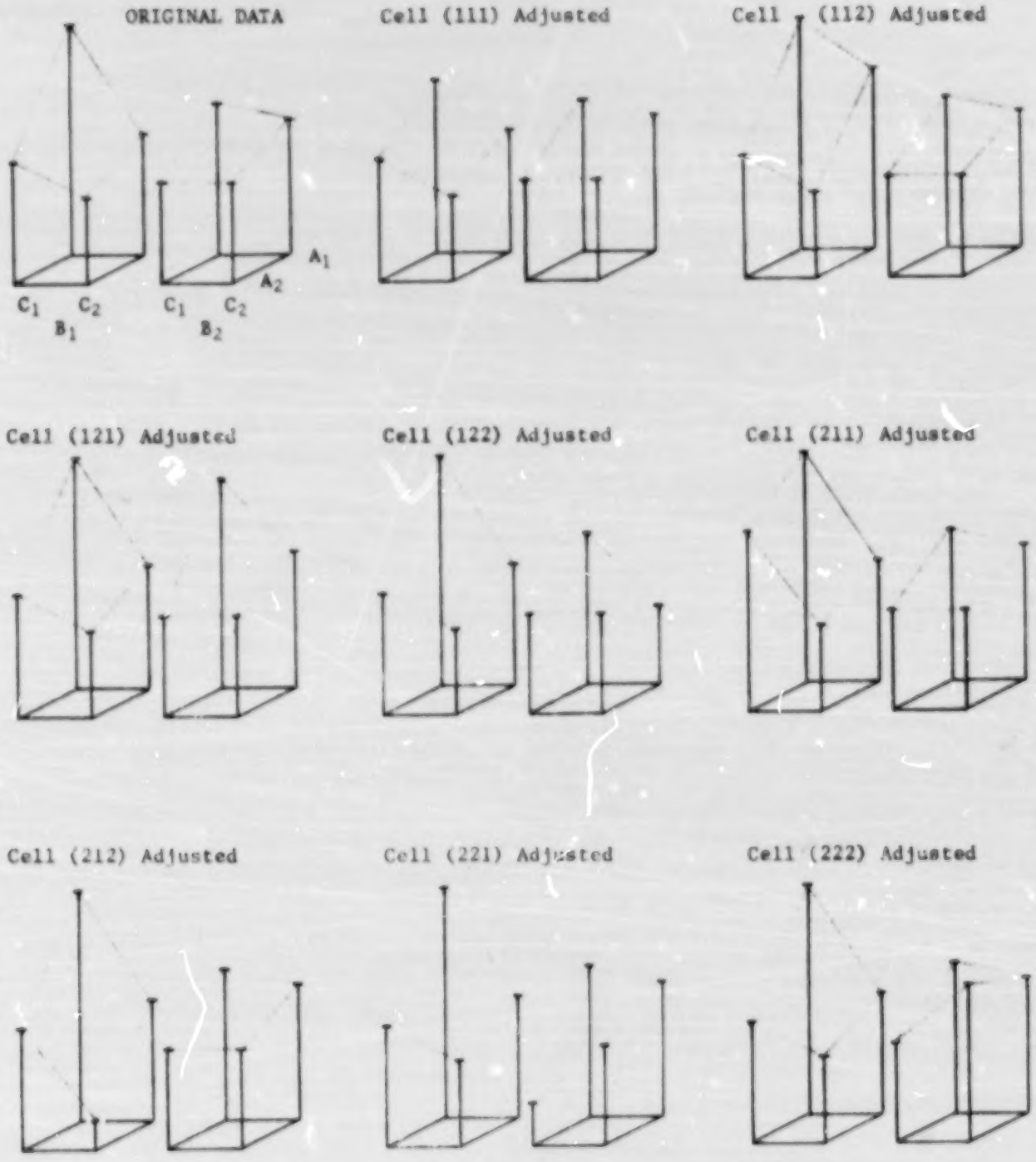

FIGURE 2. An Empirical Example (adapted from Bracewell & Hidi, 1973). Data from Table 2.

TABLE 3.
Rules of Thumb for Detecting Synergistic Effects

A. 2^k Designs.

1. Write each source of variation as a formal contrast.

2. Choose some source of variation which "ought" not to exist (by reason of parsimony, theoretical argument, or intuition, for example) and for which a small, preferably non-significant, mean square is reported in the original analysis. Often the source chosen will be the k-way interaction. (Alternatively, choose the source of variation having the smallest reported mean square.)

3. Set the contrast associated with the selected source to zero.

4. Solve that contrast for each cell mean in turn (given the other cell means) to obtain an "adjusted" mean as an estimate of the cell mean that would have been obtained in the absence of synergy.

5. For each cell mean in turn, recalculate the ANOVA using the "adjusted" value for the cell in question. (This implies 2^k separate analyses.) Examine the resulting patterns of "significant" effects.

6. Consider the implications of a synergy in each cell: in theoretical terms, in terms of the pattern of "significant" effects found when the cell mean is adjusted, and in terms of the total sum of squares for treatments (SS_{Tr}) obtained as a result of that adjustment.

7. Retain as tenable working hypotheses any hypothetical synergies for which (i) the pattern of "significant" effects is more readily interpretable than the original pattern; (ii) the total SS_{Tr} is less than the original value; and (iii) the non-significant effects have in general smaller mean squares than in the original analysis.

B. General Factorial Designs.

1. Write each source of variation as a set of orthogonal contrasts.

2. Choose some source of variation whose sum of squares is to be minimized. (Bases for selection include (i) the smallest reported mean square; (ii) theoretical arguments, or parsimony, implying that the selected source of variation ought to be negligible; (iii) intuition; (iv) combinations of (i)-(iii).)

3. Minimize the SS for the selected source of variation, with respect to the mean of one cell in the design; solve for the value of that "adjusted" mean.

4. Recalculate the ANOVA, substituting the "adjusted" mean for the observed value. Examine the resulting pattern of "significant" effects.

5. Consider the implications of a synergy (or synergistic effect) in the cell selected for adjustment in terms of theory, of the pattern of "significant" effects found after adjustment (as compared with that observed before adjustment), and of the total SS_{Tr} obtained as a result of adjustment.

6. Repeat steps 3-5 above for every other cell in the design.

7. Retain as tenable working hypotheses any hypothetical synergies for which (i) the pattern of "significant" effects is simpler and more readily interpretable than the unadjusted pattern; (ii) the total SS_{Tr} is smaller than the unadjusted value; and (iii) the non-significant effects have in general smaller mean squares than in the original analysis.

[Notice that procedure B can be immediately extended to minimize several sources of variation simultaneously, if desired.]